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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,842	04/30/2001	Akira Murasugi	SPO-112	1096
7590 12/17/2003			EXAMINER	
David R Saliwanchik Suite A 1 2421 NW 41st Street Gainesville, FL 32606-6669			QIAN, CELINE X	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/762,842	MURASUGI ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Celine X Qian	1636	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 15 September 2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 8 and 10-12 is/are rejected.
- 7) ☒ Claim(s) 6, 7, 9, 13 and 14 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                               | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>0303,0503</u> | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

Claims 1-14 are pending in the application.

This Office Action is in response to the Amendment filed on 9/15/03.

#### ***Response to Amendment***

The Objection to the specification for lacking page numbers has been withdrawn in light of Applicant's submission of substitute specification.

Acknowledgement is made of Applicant's submission of supplemental sequence listing. The application is now in sequence compliance.

The rejection of claims 6, 7, 9, 13 and 14 under 35 U.S.C.112 1<sup>st</sup> paragraph has been withdrawn in light of Applicant's argument.

The rejection of claims 5-9 and 11-14 under 35 U.S.C.112 2<sup>nd</sup> paragraph has been withdrawn in light of Applicant's amendment of the claims.

The objection to drawing is maintained for reasons discussed below.

The rejection of claims 1-4 and 10 under 35 U.S.C.112 2<sup>nd</sup> paragraph is maintained for reasons set forth of the record mailed on 2/14/03 and further discussed below.

The rejection of claims 1-5, 8 and 10-12 under 35 U.S.C.103 (a) is maintained for reasons set forth of the record mailed on 2/14/03 and further discussed below.

#### ***Response to Arguments***

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "5' and 3' sequences within the AOX1 gene" renders the claims indefinite because it is unclear which part of AOX1 gene Applicants are referring to. It is unclear whether it is referring to 5' and 3' un-translated region of the AOX1 gene or the coding sequence. In addition, if it is within the coding region, then at which position of the nucleotide is considered to be 5' or 3'. As such, the metes and bounds of the claim cannot be established.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-5, 8 and 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al (WO 92/13951), in view of Tomomura et al (1990, JBC, Vol. 265, No. 18, pp. 10765-10770) and Li et al (1990, Science, Vol.250, pp.1690-1694).

In response to this rejection, Applicants argue that the claimed vector possesses a unique feature which involves the ligation of the MK protein cDNA downstream of the  $\alpha 1$  factor gene under the regulation of the AOX1 promoter from *P.pastoris*. Applicants assert that such unique feature resulted in increased production of MK protein which is an unexpected result.

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Applicants further argue that Davis et al. teaches away from the present teaching because it suggested that the secretion signal may be selected either from the  $\alpha 1$  factor or native protein secretion signal. In addition, Applicants argue that the selection of a specific pH value (pH3) is important for the success of the claimed invention which the prior art fails to teach. Applicants thus conclude that the cited references do not render the invention obvious because they do not teach a motivation to combine and an reasonable expectation of success.

These arguments have been fully considered but deemed unpersuasive. The teaching of Davis, Tomomura and Li et al. and reasons for the obviousness rejection were discussed in detail in the previous office action (see pages 5-8). In response to Applicant's response about unexpected results, Applicants are reminded that the rejected claims do not recite such limitation. The claims are drawn to a vector for secretory expression of MK family protein, yeast transformants comprising said vector, and a method of producing MK protein by culturing said transformants. All the components of the vector are taught by the combined teaching of Davis, Tomomura and Li. None of these claims recites any limitation of increased production or producing the MK protein at a specific pH. Therefore, the combined references are not required to teach these limitation to render the invention obvious.

Contrary to Applicants' assertion, Davis et al do not teach away from the claimed invention just because it teaches that the secretory signal can be either  $\alpha 1$  factor or native protein secretion signal. Teaching both secretory signals can be used does not exclude one from another. Therefore, this argument is not persuasive.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the

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teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation to combine is clearly set forth in the teaching of the references as discussed previously that the expression system taught by Davis et al. would overcome the major problems associated with *S. cerevisiae* expression system such as loss of selection for plasmid maintenance and distribution. The level of skill in the art of molecular cloning and protein expression is high. It would be routine for one of ordinary skill of art to make the claimed vector and transfer into a yeast strain for protein expression. Therefore, the claimed invention is obvious in view of the cited references, and the rejection is maintained.

### ***Drawings***

The drawing submitted on 8/18/03 is received. However, they are not entered because no drawing was received at the time the application was filed under 35 U.S.C. 371. Applicants should remove all references to the drawings from the specification. Alternatively, Applicants may file a petition to have the drawings entered.

### ***Conclusion***

Claims 6, 7, 9, 13 and 14 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

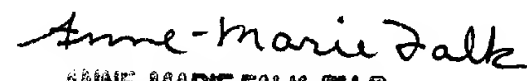
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.

  
ANNE-MARIE FALK, PH.D.  
PRIMARY EXAMINER